PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference JF/hWCM.96	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/05412	International filing date *(day/month/year)* 11.12.2003	Priority date *(day/month/year)* 19.12.2002
International Patent Classification (IPC) or both national classification and IPC C12Q1/68		
Applicant UNIVERSITY OF WALES COLLEGE OF MEDICINE et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.01.2004	24.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Brochado Garganta, M Telephone No. +49 89 2399-8935

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/05412

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-44 as originally filed

Claims, Numbers

1-8 as originally filed

Drawings, Sheets

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-8
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-8
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: CHASMAN D ET AL: "Predicting the functional consequences of non-synonymous single nucleotide polymorphisms: structure-based assessment of amino acid variation" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 307, no. 2, 23 March 2001 (2001-03-23), pages 683-706, XP004466046 ISSN: 0022-2836

D2: PAYSEUR B A ET AL: "Natural selection at linked sites in humans" GENE: AN INTERNATIONAL JOURNAL ON GENES AND GENOMES, ELSEVIER SCIENCE PUBLISHERS, BARKING, GB, vol. 300, no. 1-2, 30 October 2002 (2002-10-30), pages 31-42, XP004396733 ISSN: 0378-1119

D3: REICH D E ET AL: "On the allelic spectrum of human disease" TRENDS IN GENETICS, ELSEVIER, AMSTERDAM, NL, vol. 17, no. 9, 1 September 2001 (2001-09-01), pages 502-510, XP004303291 ISSN: 0168-9525

2. Novelty

The subject-matter of claims 1-8, relating to a method for identifying mutations and/or polymorphisms, to a method for detecting a haplotype and to a haplotype, is not new in the sense of Article 33(2) PCT, as such a subject-matter is already known from D1-D3.

D1 discloses a method for predicting the functional consequences of non-synonymous SNPs, wherein a structure-based assessment of amino acid variation is performed (see pages 683-690 and 694-705). *In predicting the functional consequences of such SNPs,*

the determination of those mutations particularly affecting the phenotype is being done.

D2 discloses an approach for distinguishing between background selection and genetic hitchhiking based on the relationship between polymorphism level and recombination rate for neutral loci with high mutation rates, relative levels of variation on the X chromosome and the autosomes, the frequency distribution of neutral polymorphisms, and population-specific patterns of genetic variation (see pages 31- 39).

D3 discloses the characterisation of allelic spectra of human diseases (see pages 502-509).

Using the statistical methods mentioned in D1-D3, indeed is the variation within a group, which is being determined. However, it would be possible to the skilled person, based on such models, to determine or predict where to find other significant or interesting mutations.

3. Claim 8 is not clear (Article 6 PCT), as the haplotype is only characterised by the method used for identifying it. Based on this feature it is impossible to characterise all the possible haplotypes, which could fall into the scope of this claim.